Massachusetts Department of Public Health

State Laboratory Institute

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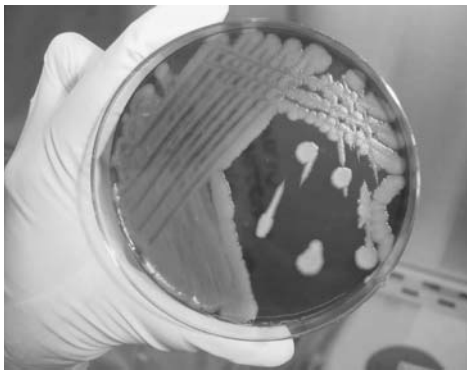
Bioterrorism Preparedness Training for Clinical Microbiology Labs

Laboratory based infectious disease surveillance systems that detect and identify naturally occurring events also aid early warning of bioterrorism. The U.S. Centers for Disease Control and Prevention (CDC) and State Public Health Laboratories (SPHL) in collaboration with the SPHL's member organization, the Association of Public Health Laboratories (APHL), developed a comprehensive model to enable effective collaboration for bioterrorism preparedness and response. This new initiative is the Laboratory Response Network (LRN). The LRN endeavors to strengthen federal, state and local public health laboratories and improve communication and technical cooperation among them. LRN also seeks to improve communication and cooperation between the public health laboratories and clinical microbiology laboratories, to support strengthening of their capabilities and capacities, and to collaborate with the broad alliance of partners with critical roles in bioterrorism.

The LRN involves four levels of activity, Levels A, B, C and D, with Level D performing the most complex testing of high-risk agents. Level A consists of microbiology laboratories that can detect critical infectious agents by primary culture supplemented by presumptive rule-in/rule-out testing. Level B consists of those public health laboratories that perform confirmatory testing on specimens received from Level A. Level C laboratories are advanced capability public health labs capable of performing a broad spectrum of advanced testing including determination of drug susceptibility and strain typing. Finally, Level D laboratories consist of federal laboratories that develop new testing methods and provide advanced testing and confirmation services. Level D laboratories also provide biohazard level 4 facilities if required. All laboratories in the network are knowledgeable about the safe handling of infectious agents within the laboratory and how to properly package and ship infectious agents.



B. anthracis on blood agar

As a Level C Laboratory, the Massachusetts State Laboratory Institute (SLI) offers training to microbiologists in the more than 100 Level A laboratories performing diagnostic microbiology testing within the state. This training course consists of lecture and laboratory components. Those attending earn 0.45 continuing education credits. These individuals also receive an instruction manual that can be used to educate laboratory staff when attendees return to their respective facilities.

Oral and visual presentations emphasize performance criteria for successful presumptive testing for *Bacillus anthracis, Yersinia pestis, Francisella tularensis,* and *Brucella species*. The presentation is supplemented with a collection of digital images showing typical laboratory findings and clinical manifestations of the disease states. Emphasis throughout is placed on safety requirements compliant with all regulatory agencies for laboratory manipulation of these organisms and packaging/transportation of organism isolates to the state laboratory for advanced testing. Included are communication protocols and contact information for reporting significant findings and requesting information as well as a summary of resources regarding the subject of bioterrorism for use in preparedness

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Bioterrorism Preparedness Training for Clinical Microbiology Labs

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planning and staff education. Questions and discussion are encouraged throughout.

The laboratory component of the training includes familiarization with a Biosafety level 3 facility at SLI. There participants are able to get hands on experience with representative cultures of the relevant organisms, as they would appear on commonly used laboratory media after varying lengths of incubation. Performance of presumptive testing is demonstrated and participants are able to perform some of the tests during the session. Prepared smears are presented via real time digital closed circuit monitor to allow group instruction and discussion.

Programs to meet additional training needs will be offered in the coming months. Classes will present laboratory procedures currently in development for other organisms that will allow level A laboratories to broaden their screening capabilities. Sessions will also be designed to refresh laboratory staff on material that has already been presented and provide training to alternate representatives of facilities that have already participated. New methods to be offered in training will include a rule-in test for varicella virus infection (chickenpox).

Questions about training opportunities and requirements can be addressed to Garry Greer, State Laboratory Training and Distance Learning Coordinator, at 617-983-6608 or Peter Belanger, Biological Threat Laboratory Coordinator, at 617-983-6267.

Caution Against the Use of Hand-Held Assays in the Field for Presumptive Rule-out or Rule-in of Infectious Agent

This issue of the SLI Newsletter reprints the recent recommendation from the U.S. Department of Health and Human Services (DHHS) that federal agencies are not to purchase hand-held kits, which are used for the presumptive rule-out or rule-in of infectious agents that may be suspected to be present in materials such as common white powder-like material found in various home and business environments. The DHHS recommendation is based on the performance characteristics of the assays, as well as the likelihood of the presence or absence (prevalence) of the infectious agent in the materials being tested, and the conclusion that the predictive value of these assays for this particular purpose is poor. The State Laboratory Institute agrees with this recommendation.

SLI can provide 24/7 rapid testing of suspicious materials to rule-out or rule-in infectious agents in situations that are potential terrorist events.

SLI emphasizes the problematic issues that result in low predictive value for test results from the use of hand-held assays in the field, and the importance of threat analysis by law enforcement in deciding if material should be tested. Common practice of many first responder groups that use hand-held assays can result in incorrect results and poor predictive value for both positive and negative test results. In addition to the lower sensitivity and specificity of hand-held assays compared to conventional instrumental rapid assays, the common practice of how these assays are used is problematic and is worth emphasis.

Testing when there is no credible suspicion of risk. The most frequent event is an individual's report of material that has contaminated or tainted some item or surface, and the worry that the material may be infectious. The majority of these reports involve events that have no credible associated risk or threat. Testing these materials, especially using hand-held assays that have lower specificity, results in the same problem that occurs if a low specificity test for an infectious agent is used for screening a population with a low prevalence for the disease, an unacceptable rate of false positives. A false positive screening test obtained in the field can result in actions and interventions that are unnecessary and even harmful.

Testing when there is a credible suspicion of risk. When there is a credible threat or risk that has been identified, such as a threat letter, standard procedures require a timely response and definitive rule-out or rule-in of the risk. Because hand-held assays are less sensitive than laboratory-based technology, there is a much greater chance of a false negative test result, which can result in incorrect recommendations and a failure to implement precautions to adequately prevent disease.

Questions concerning risk assessment can be referred to 617-983-6800, and questions on testing to 617-983-6607.

STATEMENT BY THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Regarding Hand-Held Assays for Identification of *B. anthracis* Spores

Purpose

To provide law enforcement, fire services, emergency managers and other first responders with guidance regarding the purchase and use of hand-held assays used for detecting anthrax spores and other biological agents.

Summary

The U.S. Department of Health and Human Services at this time recommends against use by first responders of hand-held assays to evaluate and respond to an incident involving unknown powders suspected to be anthrax or other biological agents.

Background

In recent months, Federal, State and local first responders have had to evaluate numerous samples of white powdery substances to determine if *B. anthracis* (anthrax) spores are present. In some cases, field tests showed an apparent "positive" result and this led to the quarantine, isolation or decontamination of people. When these samples were referred to a reference lab in the Laboratory Response Network (LRN), they were found to be negative through microbiological culturing and molecular methods. The devices used for the initial field tests included tickets and strips from at least four vendors. Problems resulted from a variety of factors, such as testing of caustic or harsh chemicals or the performance of tests by inadequately trained personnel.

Discussion

Biological agent field test kits are, at this time, not sufficiently accurate for on-scene decision making in the field. Besides the high number of false positive results, hand-held assays also yield negative results on samples that are truly positive (false negatives). In formal terms, the sensitivity of such assays is in the range of 100,000 spores whereas a culture may detect one spore.

In contrast to situations with chemical exposure where rapid decision making (minutes) can be crucial to the protection and treatment of individuals, there are no examples of biological exposure where decision-making cannot wait for the results of validated laboratory procedures (1-2 days). Any perceived benefit of using currently available hand-held assays falls short of the costs of unnecessary remedial actions and amplified public concern.

No Federal agency certifies or approves these devices. The FBI and CDC have recently evaluated commercially available hand-held assays for the detection of *B. anthracis*. These studies confirm the low sensitivity of such assays and their potential to produce false-positive results with non-anthrax bacteria and chemicals. The performance of handheld assays for the detection of biological agents other than *B. anthracis* has not been evaluated and their use is also not recommended at this time.

Conclusions

Until results are obtained that would warrant the use of hand-held assays, DHHS recommends:

(1) hand-held assays systems not be used for the assessment of suspected biological samples;
(2) whenever a biological agent is suspected, a unified command should assess the credibility of the situation and determine an appropriate response. The unified command should include fire services, public health, the FBI's Weapons of Mass Destruction Coordinator, and law enforcement;
(3) substances that are found to be a credible public health threat by the unified command should be screened in the field for volatile organic compounds (VOC), pH, explosives, and radiation, and then sent to an appropriate laboratory in the Laboratory Response Network (LRN) for testing. First responders and local public health programs need to establish protocols to provide this support and logistics of the response. Besides testing of samples in an LRN laboratory, the protocol should include a system for identification and follow-up of the potentially

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Norwalk-like Virus Testing at SLI

The PFGE laboratory received funding in April though the Enhanced Laboratory Capacity (ELC) cooperative agreement to provide RT-PCR testing for the presence of Norwalk like Virus (NLV). NLV and other caliciviruses are considered to be the most common cause of gastrointestinal illness associated with foodborne outbreaks. (MMWR 50 (RR09); 1-18, 2001, JID 186: 1-7, 2002) NLV testing capability will be a significant benefit to the Enteric lab and state epidemiologists where foodborne illness is suspect and no enteric bacterial pathogens have been found, which often happens.

The symptoms of NLV infection are nausea, camps, vomiting and diarrhea, sometimes accompanied by low-grade fever and headache (http://www.cdc.gov/od/oc/media/fact/norwalkv.htm). Onset is acute and recovery usually occurs in 2-3days. NLV is an RNA virus and can be found in the stool of persons with an active infection. In the past, the virus was identified morphologically by electron microscopy. Because very few laboratories had this capability and because of the transient nature of NLV infection, accurate identification of NLV in foodborne outbreaks was limited.

The RT-PCR test method the PFGE laboratory uses to identify NLV was developed at the CDC 's Viral Gastroenteritis Section and is used by eleven state laboratories. To validate testing for NLV, all specimens will be retested by the CDC until the laboratory establishes proficiency in the method. Specimens positive for NLV are further sequenced by the CDC. The sequence data provides a fingerprint of the particular genotype of the virus and will allow more accurate monitoring of NLV and related outbreaks. This data will eventually be available to participating state health laboratories through CaliciNet, an electronic network of sequence data, which will allow states to directly input their data and immediately receive notification of matching sequences in the database.

Because the presence of NLV in the stool of an infected individual can be short-lived, it is essential to get clinical specimens in to the lab for testing a soon as possible. Specimens must be obtained within 48 hrs of the onset of symptoms and kept cold during transit to the PFGE laboratory. If an outbreak of NLV is suspected, local boards of health or clinical microbiology laboratories should contact state epidemiologists (617-983-6800) who will determine if testing is warranted. Arrangements will then be made with the PFGE laboratory to coordinate the collection and receipt of the specimens.

In May the PFGE laboratory identified NLV in stools of patrons and food handlers involved in several simultaneous outbreaks of severe gastrointestinal illness. The results were confirmed by the CDC. These outbreaks provided the PFGE laboratory with an opportunity to begin validation of the RT-PCR test for NLV.

STATEMENT BY THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Regarding Hand-Held Assays for Identification of *B. anthracis* Spores

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exposed population and a joint communication plan for the public and media relations. Since exposure to airborne anthrax spores is potentially life threatening, all credible threats should be handled appropriately in a timely manner.

References:

1. "CDC Health Advisory: Hand-Held Immunoassays for Detection of *Bacillus anthracis* Spores." October 18, 2001 http://www.bt.cdc.gov/DocumentsApp/Anthrax/10182001HealthAlertPM/10182001HealthAlertPM.asp

2. "Use of Onsite Technologies for Rapidly Assessing Environmental *Bacillus anthracis* Contamination on Surfaces in Buildings."
CDC MMWR Vol 50 Number 48.
December 7, 2001.
http://www.cdc.gov/mmwr/PDF/wk/mm5048.pdf

3. "Approved Tests for the Detection of *Bacillus anthracis* in the Laboratory Response Network."
http://www.bt.cdc.gov/DocumentsApp/Anthrax/ApprovedLRNTests.asp

Laboratory Testing of *Bacillus anthracis*

The introduction of *Bacillus anthracis* into the United States postal system during the fall of 2001 resulted in thousands of test requests to SLI of items suspected of contamination. Although procedures for testing biological threat specimens were previously in place, aspects of submission, testing and reporting required modification due to the unexpected quantity and the characteristics of many of the environmental specimens.

Biological threat specimens are often submitted to the laboratory by first responders such as police, fire and HazMat units as well as local boards of health. Due to the large volume, a specimen receiving station was created within the front doors of SLI. Specimens were then transported directly to a Biosafety level 3 laboratory separate from the flow of standard laboratory specimens.

During the months of October and November 2001, the laboratory tested 40-70 specimens per day, 7 days per week. Of the approximately 3,000 environmental specimens submitted for *B. anthracis* testing in Massachusetts thus far, less than 1% are associated with an identifiable threat such as a letter or suspicious powder (Table 1). Approximately 40% of submitted specimens were mail related, and less than half of these contained a powdery substance. Many specimens contained a common powdery material that was readily identifiable by visual inspection. Nevertheless, all specimens submitted were tested by standard laboratory procedures for the presence of infectious agents. Specimens consisting of suspicious powders or other materials made up a minority of the submitted materials. Some specimens, which were notable for their lack of suspicion or disease risk, presented processing or analytical challenges, e.g., Christmas decorations, VCRs, frozen turkeys, and U.S. currency. All specimens submitted from Massachusetts tested negative for *B. anthracis*.

Table 1: Suspect Biological Threat Specimens Submitted to the Massachusetts State Laboratory Institute (n= >3,000*)

Specimen Description	Proportion of Total (%)
Specimens associated with a threat	<1%
Specimens not associated with a threat	
Mail	
Powder present	14%
No powder present	27%
Non-mail	
Powder present	29%
No powder present	29%

* All specimens tested negative for *Bacillus anthracis*.

National Laboratory Training Network - Update

by Betsy Szymczak

The National Laboratory Training Network (NLTN) is a CDC sponsored program managed through the Association of Public Health Laboratories (APHL). NLTN provides continuing education opportunities for those working in both public health and clinical laboratories. The training includes workshops, laboratory intensives, teleconferences, videoconferences and satellite broadcasts. To see our current list of upcoming programs go to www.nltn.org then click on Laboratory Training Courses.

The NLTN Northeast Office services a 12-state region including New England, New York, Pennsylvania and the coastal states extending to Washington DC. By working closely with State Training Coordinators, the NE Office staff is able develop training opportunities to meet each state's needs. The NLTN Northeast Office is fortunate to be hosted by the Massachusetts State Laboratory Institute in Jamaica Plain. To reach us by phone call 1-800-536-NLTN, fax 617-983-8037 or email at neoffice@nltn.org.

NLTN also supports an extensive lending library with over 1,000 titles. Until recently this library could only be accessed using a paper index. Web-base access to the library was initiated three months ago. Use of the library is free and can be accessed with the following url www.phppo.cdc.gov/libnltn. Questions about the library should be directed to Denise McFadden at dmcfadden@nltn.org or 617-983-6285 or 1-800-536-NLTN.

New Faces at NLTN

by Betsy Szymczak

Almost two years ago the NLTN Northeast region expanded to include New England, New York and the Mid-Atlantic States. As NLTN implements a national restructuring plan, the Northeast Office also acquired new staff. **Shoolah Escott** former NLTN Regional Coordinator is now CDC Training Advisor for the NE office. **Betsy Szymczak** joined the office in January of this year replacing Shoolah and now serves as Manager of the NLTN Northeast Region. Betsy had previously held faculty appointments in the Medical Technology Program at several local academic institutions. This spring **Denise Korzeniowski** joined the office as NLTN Training Associate. Denise, a clinical microbiologist, has many years of experience in Boston area teaching hospitals. **Denise McFadden**, our new Program Assistant, grew up in Britain and recently received a BA from Boston University. **Pam Hodge** has been working in a part-time capacity for almost two years. Pam, a Medical Technologist, comes from an extensive training background at Instrumentation Laboratories. The NLTN NE office can be reached at 1-800-536-NLTN or neoffice@nltn.org. The newly renovated office is located on the second floor of the State Laboratory Institute.

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